Closure of the arteriotomy after carotid endarterectomy: Patch type is related to intraoperative microemboli and restenosis rate

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Objective: **Patch closure after carotid endarterectomy (CEA) improves clinical outcome compared with primary closure. Whether there are differences in outcome between various patch materials is still not clear. The objective of this retrospective study was to investigate whether a relationship exists between the patch type and the number of microemboli as registered during CEA by transcranial Doppler imaging, the clinical outcome (transient ischemic attack and cerebrovascular accident), and the occurrence of restenosis.**

Methods: **We included 319 patients who underwent CEA. Intraoperative microembolus registration was performed in 205 procedures. Microembolization was recorded during four different periods: dissection, shunting, clamp release, and wound closure. The decision to perform primary closure or to use a patch for the closure of the arteriotomy was made by the surgeon, and Dacron patches were used when venous material was insufficient. Cerebral events were recorded within the first month after CEA, and duplex scanning was performed at 3 months (n = 319) and 1 year (n = 166) after CEA. A diameter reduction of more than 70% was defined as restenosis.**

Results: **Primary, venous, and Dacron patch closures were performed in 83 (26.0%), 171 (53.6%), and 65 (20.4%) patients, respectively. Primary closure was significantly related to sex (Dacron patch, 35 men and 30 women; venous patch, 108 men and 63 women; primary closure, 72 men and 11 women; $P < .001$). The occurrence of microemboli during wound closure was also related to sex (women, 2.5 ± 0.6; men, 1.0 ± 0.2; $P = .01$). Additionally, during clamp release, Dacron patches were associated with significantly more microemboli than venous patches (11.1 ± 3.4 vs 4.0 ± 0.9; $P < .01$), and this difference was also noted during wound closure (3.1 ± 0.9 vs 1.4 ± 0.4; $P < .05$). Transient ischemic attacks and minor strokes after CEA occurred in 5 (2.4%) of 205 and 6 (2.9%) of 205 procedures, respectively, and the degree of microembolization during dissection was related to adverse cerebral events ($P = .003$). In contrast, the type of closure was not related to immediate clinical adverse events. However, primary closure and Dacron patches were associated with an increase in the restenosis rate compared with venous patches: after 400 days, the restenosis rate for Primary closure was 11%, Dacron patch 16%, and venous patch 7% ($P = .05$; Kaplan-Meier estimates).**

Conclusions: **Microemboli are more prevalent during clamp releases and wound closure when Dacron patches are used. Additionally, the observed differences in embolization noted by patch type were mainly evident in women. However, the use of Dacron patches was not related to immediate ischemic cerebral events but was associated with a higher restenosis rate compared with venous patch closure. This suggests that venous patch closure may be preferred for CEA. (J Vasc Surg 2005;42:1082–8.)**

A recent systematic review concerning the type of arteriotomy closure in carotid endarterectomy (CEA) showed the benefits of patching over primary closure.[1] However, sufficient data are lacking to allow firm conclusions to be drawn regarding differences between various patch materials used for carotid closure. Synthetic patches are believed to be more thrombogenic than venous patches and may therefore theoretically produce emboli that could result in associated adverse cerebral events.

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Competition of interest: none.

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During CEA, transcranial Doppler (TCD) registration of the middle cerebral artery provides online surveillance of hemodynamic changes and the passage of cerebral microemboli,[2-4] and the occurrence of microemboli, recorded by TCD during CEA, has been related to the risk of immediate adverse cerebral events.[3,5,6] Therefore, different patch materials could influence the outcome of the operation as a result of differences in the number of microemboli.[7] Furthermore, several studies suggest that the type of patch used for closure of the carotid artery is also associated with late restenosis.[1,7-12] The objective of this study was to investigate whether a relationship exists between the type of patch used, the number of TCD-detected microemboli during CEA, immediate adverse cerebral events, and restenosis.

METHODS

Patients. This study is part of ATHERO-EXPRESS, which is an ongoing prospective longitudinal study with

the objective of investigating the etiologic value of plaque characteristics in long-term outcome in patients with carotid atherosclerosis. The design of the study has been described previously,[13] and ATHERO-EXPRESS is currently being executed in two Dutch hospitals. Recruitment of patients started in April 2002 and will continue until at least 1000 patients have been included. All patients receiving operative treatment for carotid stenosis in the vascular surgery departments of the participating centers are enrolled. Patients can be symptomatic or asymptomatic, and surgery is indicated when color Doppler–assisted duplex ultrasound investigation, magnetic resonance angiography, computed tomographic angiography, or angiography reveals a diameter reduction of more than 70% on at least one side. In asymptomatic patients with stenosis greater than 70%, the indication for surgery is also based on recommendations published by the Asymptomatic Carotid Surgery Trial.[14] At baseline, clinical data from patients' records, a questionnaire about medical history, blood samples, and atherosclerotic tissue harvested during CEA are collected. In this study, we analyzed 319 patients with 3 months and 1 year (n = 166) of follow-up after CEA.

Carotid endarterectomy. Preoperative antiplatelet therapy was continued during the operation. All patients underwent operation under general anesthesia, and TCD and electroencephalographic monitoring were used. Shunting was performed selectively on the basis of electroencephalogram and TCD criteria, as described in previous articles.[15,16] Before cross clamping, a bolus of heparin (5000 IU) was given intravenously. All endarterectomies were performed open, with dissection of the bifurcation into the internal and external carotid arteries. Patch closure was generally the preferred technique, especially when the lumen of the internal carotid artery was less than 3 mm or when a shunt had to be used. Venous patches were preferred and were usually obtained from the saphenous vein at the ankle or inguinal level when the vascular surgeon favored patch closure. A Dacron patch (Intervascular; DuPont, Wilmington, Del) was used only when venous material was not available or when the venous material harvested was perceived to be of insufficient strength. The medical ethics committees of the participating hospitals approved the study.

TCD monitoring. Because of logistic reasons, it was not always possible to record emboli to the highest standard during TCD recording. Therefore, we reported the TCD registrations of 205 of 319 patients. The methods of TCD monitoring have been reported previously.[15,16] Briefly, the Doppler spectra were observed online in the operating room by an experienced sonographer. Doppler signals were recorded, and high-intensity transient signals indicating microemboli were identified. All microembolic events were counted and recorded during four different phases of the surgical procedure: (1) dissection (all microembolic events from skin incision until cross clamping), (2) shunting (if a shunt was used; microemboli that occurred from the introduction to the removal of the shunt), (3) clamp release (the first 10 seconds after restoration of the flow through the carotid arteries), and (4) wound closure (after 10 seconds of flow restoration until the end of the operation). Observed microemboli that could not be counted separately during one heartbeat were entitled *shower microemboli*. A shower of microemboli was given the arbitrary number of 10 microemboli, which is the maximum number of microemboli that can be discriminated during 1 heartbeat.

Clinical events. Patients' hospital records were reviewed to obtain information concerning clinical events. A neurologist was routinely consulted for all patients before surgery and at the third day after operation. New neurologic symptoms or worsening of existing symptoms that persisted for longer than 24 hours was regarded as a stroke, and strokes were classified according to the modified Rankin Scale.[17] New neurologic symptoms persisting less than 24 hours were regarded as transient ischemic attacks. Neurologic events were termed *immediate adverse ischemic cerebral events* when they were diagnosed during the postoperative period or when a readmission occurred for this reason within 1 month after the operation.

Restenosis and duplex criteria. Determination of the degree of recurrent stenosis during follow-up was based on duplex ultrasonographic[18] follow-up at 3 months (n = 319) and 1 or 2 years (n = 166) after CEA. Restenosis was defined as greater than 70% stenosis of the endarterectomy area. Duplex criteria for restenosis are a combination of peak systolic velocity greater than 125 cm/s and a gamma (the ratio between peak systolic velocity in the stenotic area and end diastolic velocity in distal common carotid artery) greater than 12.

Data analysis. Microembolic data in tables are presented as mean ± SEM. We used nonparametric tests for continuous variables (Mann-Whitney test and Kruskal-Wallis test) and χ^2 and Fisher exact tests for categorical variables. When significant differences were found with the Kruskal-Wallis test, the Dunn post hoc test was applied for their possible relationship with microemboli. Kaplan-Meier survival tables were used to assess differences in restenosis rates among groups over time. Significance was calculated with the log-rank test. All variables as displayed in the baseline table were tested for their possible relationship with restenosis and microemboli. P values of $<.05$ were considered statistically significant.

RESULTS

Primary, venous, and Dacron patch closures were performed in 83 (26.0%), 171 (53.6%), and 65 (20.4%) patients, respectively. Table I presents the baseline patient characteristics. Sex, smoking habits, and age differed significantly among groups. Additionally, closure type was related to sex; primary closure was significantly less common in women (Dacron patch, 35 men and 30 women; venous patch, 108 men and 63 women; and primary closure, 72 men and 11 women; $P < .001$).

Dacron patch use was associated with significantly more microemboli compared with venous patches and primary closure during the clamp-release phase and the

Table I. Baseline patient characteristics

Variable	*Dacron patch*	*Vein patch*	*Primary*	*Overall*	P *value*
Male sex	54% (35/65)	63% (108/171)	87% (72/83)	215/319	<.001
Age, y, median (range)	67 (45-87)	66 (40-84)	70 (55-85)	68 (40-87)	.004
Current smoker	18% (10/57)	32% (51/157)	18% (14/80)	75/294	.013
Diabetes	18% (10/57)	19% (29/155)	19% (15/78)	54/290	.9
Dyslipidemia	65% (36/55)	63% (97/154)	55% (42/76)	175/28522	.4
Symptoms	19	76% (126/165)	73% (59/81)	7/306	.6
Left side operated on	70% (42/60)	53% (91/171)	57% (47/83)	168/319	.4
Mean body mass index (kg/m^2)	46% (30/65)	26	27	26	.8
Myocardial infarction ever	27	18% (28/153)	28% (22/80)	59/292	.14
Statin use	15% (9/59)	66% (113/170)	61% (51/83)	210/317	.4
Angina pectoris ever	72% (46/64)	40% (64/162)	41% (33/81)	118/306	.6
High blood pressure	33% (21/63)	67% (102/152)	64% (49/77)	190/288	.9
CABG or coronary stent in the past	66% (39/59)	20% (33/167)	27% (22/82)	66/312	.3
Peripheral vascular intervention in	17% (11/63)		18% (15/82)		
the past (PTA/stent or bypass)	29% (18/63)	19% (31/167)		64/312	.4
Antiplatelet or anticoagulant therapy	95% (58/61)	92% (147/160)	92% (73/79)	278/300	.7

CABG, Coronary artery bypass grafting; *PTA,* percutaneous transluminal angioplasty.

Table II. Patch and TCD-detected microemboli

Phase of CEA	*Dacron*	*Vein*	*Primary*	P *value: Dacron vs vein*	P *value: primary vs vein*	P *value: Dacron vs primary*
Clamp release						
All patients	11.1 (3.4)	4.0 (0.9)	9.8 (3.5)	<.01	NS	<.05
Male	9.8 (4.2)	4.7 (1.3)	9.9 (4.1)	NS	NS	NS
Female	13.7 (6.0)	2.8 (0.8)	9.1 (5.7)	<.01	NS	NS
Wound closure						
All patients	3.1 (0.9)	1.4 (0.4)	0.7 (0.2)	<.05	NS	<.01
Male	1.3 (0.5)	1.0 (0.4)	0.8 (0.3)	NS	NS	.08
Female	6.7 (2.1)	2.0 (0.7)	0.2 (0.1)	<.05	NS	<.01

Data are presented as mean (SEM).
TCD, Transcranial Doppler; *CEA,* carotid endarterectomy; *NS,* not significant.

wound-closure phase of CEA (Table II and Fig 1). To exclude confounding of smoking, age, and sex, the analyses were repeated for these variables. Smoking and age were not related to an increased number of microemboli during clamp release and wound closure ($P = .4/P = .9$ and $P = .9/P = .8$). In contrast, women had more microemboli observed during wound closure ($P = .01$; Table III). Additionally, the significant relationship between the type of patch used and the presence of microemboli was most evident for women (Table II), so that in women, there was clearly an increased number of recorded microemboli during clamp release and wound closure when Dacron patches were used. No such relationship was seen in men.

Adverse ischemic cerebral events (<1 month after CEA) occurred in 2.4% (transient ischemic attack) and 2.9% (minor strokes) of cases. These events were significantly associated with microemboli during dissection but not during shunting, clamp release, and wound closure (Table IV; $P = .003$). Furthermore, a relationship between patch use and immediate clinical adverse events was not observed (Dacron patch, two events; vein patch, four events; and primary closure, five events; $P = .5$).

Dacron patches were associated with an increased restenosis rate compared with venous patches: after 400 days, Dacron patch 16%, primary closure 11%, and venous patch 7% (log-rank test; $P = .05$; Fig 2). To exclude confounding for smoking, age, and sex, analyses of these results were repeated. Restenosis was equally distributed among smokers and nonsmokers and categorized age groups. In contrast, women had an increased rate of restenosis when a Dacron patch or primary closure was used (compared with vein patching), whereas men showed an increased restenosis rate for primary closure (nonsignificant for women or men separately; log-rank test; $P = .12$ and $P = .16$; significant for men compared with women; $P = .02$). All patients but one who developed restenosis were asymptomatic. Four of the patients with restenosis were treated with carotid artery stent placement (including the symptomatic patient), and one patient underwent CEA.

DISCUSSION

Carotid artery stenosis is a common presentation of atherosclerotic disease.[19] A total of 9% to 12% of patients with known atherosclerotic disease have high-grade carotid artery stenosis.[20] CEA is a widely accepted method of treating patients with significant carotid artery stenosis, and prevention of perioperative adverse cerebral outcome and reduction of restenosis could improve long-term results

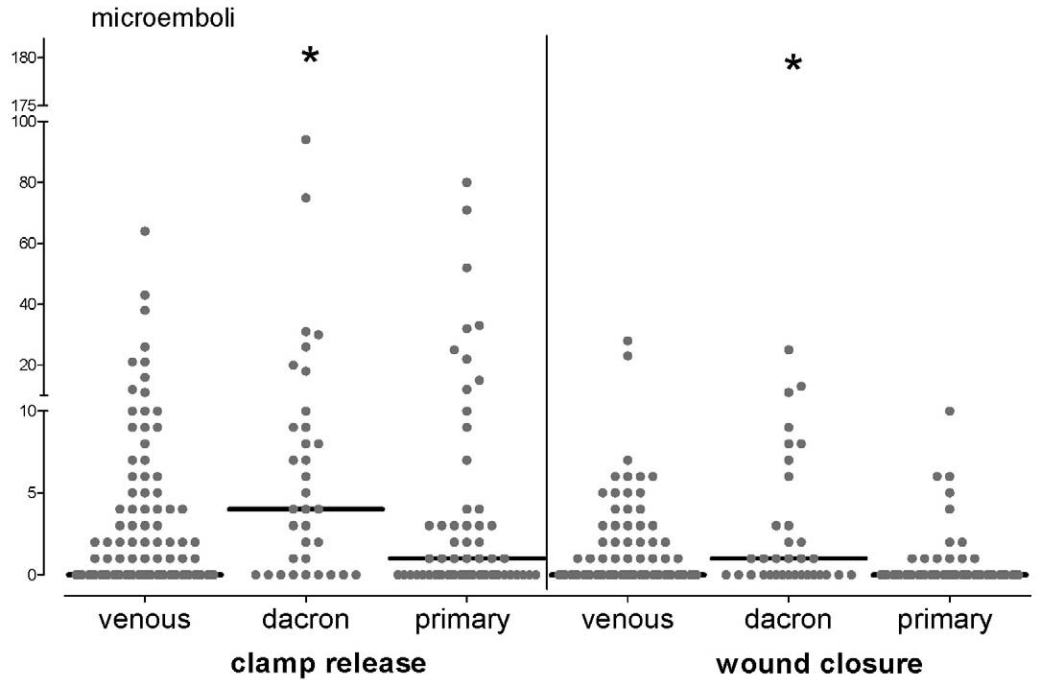

Fig 1. Relationship between microemboli recorded during clamp release and wound closure for the different kind of patches and primary closure. The Dacron patch was related to an increased number of microemboli during clamp release and wound closure. Bars indicate median (for venous patch during clamp release and also for primary closure during wound closure). Please note the y-axis scaling. *CEA,* Carotid endarterectomy.

Table III. Sex and microemboli

Phase of CEA	*Male*	*Female*	P *value*
Dissection	1.4 (0.5)	0.8 (0.2)	.87
Shunting	3.9 (0.9)	7.1 (3.2)	.60
Clamp release	7.7 (1.8)	6.2 (1.6)	.76
Wound closure	1.0 (0.2)	2.5 (0.6)	.01

Data are presented as mean (SEM).
CEA, Carotid endarterectomy.

Table IV. Microemboli in patients with and without adverse events at <2 weeks

Phase of CEA	*Stroke and TIA*	*No event*	P *value*
Dissection	6.9 (5.3)	1.1 (0.3)	.003
Shunting	4.4 (1.8)	5.3 (1.3)	.8
Clamp release	15.1 (9.0)	6.6 (1.3)	.9
Wound closure	1.3 (0.9)	1.5 (0.30)	.9

Data are presented as mean (SEM).
CEA, Carotid endarterectomy.

after CEA. Direct outcome of CEA is related to preoperative, intraoperative, and postoperative recorded microemboli.[5,21,22] Additionally, as demonstrated here, microemboli during CEA occur variably throughout the procedure and are related to sex and the type of closure used for carotid reconstruction.

Because TCD is based on ultrasonography, it is not possible to discriminate among different kinds of emboli (particles of the plaque, thromboemboli, and gaseous emboli). We assume that microemboli during dissection are mainly plaque particles and are thus associated with plaque characteristics. In contrast, during wound closure, microemboli are likely mainly thromboembolic, whereas during clamp release, microemboli are likely to be gaseous.[5] For this reason, we divided embolic events during CEA into the aforementioned categories.

The main findings of this study are as follows: (1) Dacron patches are associated with significantly more microemboli during clamp release and wound closure compared with venous patch closure and primary closure, especially in women; (2) there is a relationship between female sex and patch use, as well as with embolization and restenosis; (3) the different types of arterial closure were not associated with differences in adverse cerebral events before 1 month; (4) adverse cerebral events were associated with more microemboli during the dissection phase but not during shunting, clamp release, or wound closure; and (5) venous patch use was associated with a decreased long-term restenosis rate.

Embolism is the principal cause of cerebrovascular complications from CEA.[2] Prevention of embolic events should contribute to a decrease in adverse cerebral events. Not only emboli occurring during dissection of the atherosclerotic plaque are associated with an increased risk of

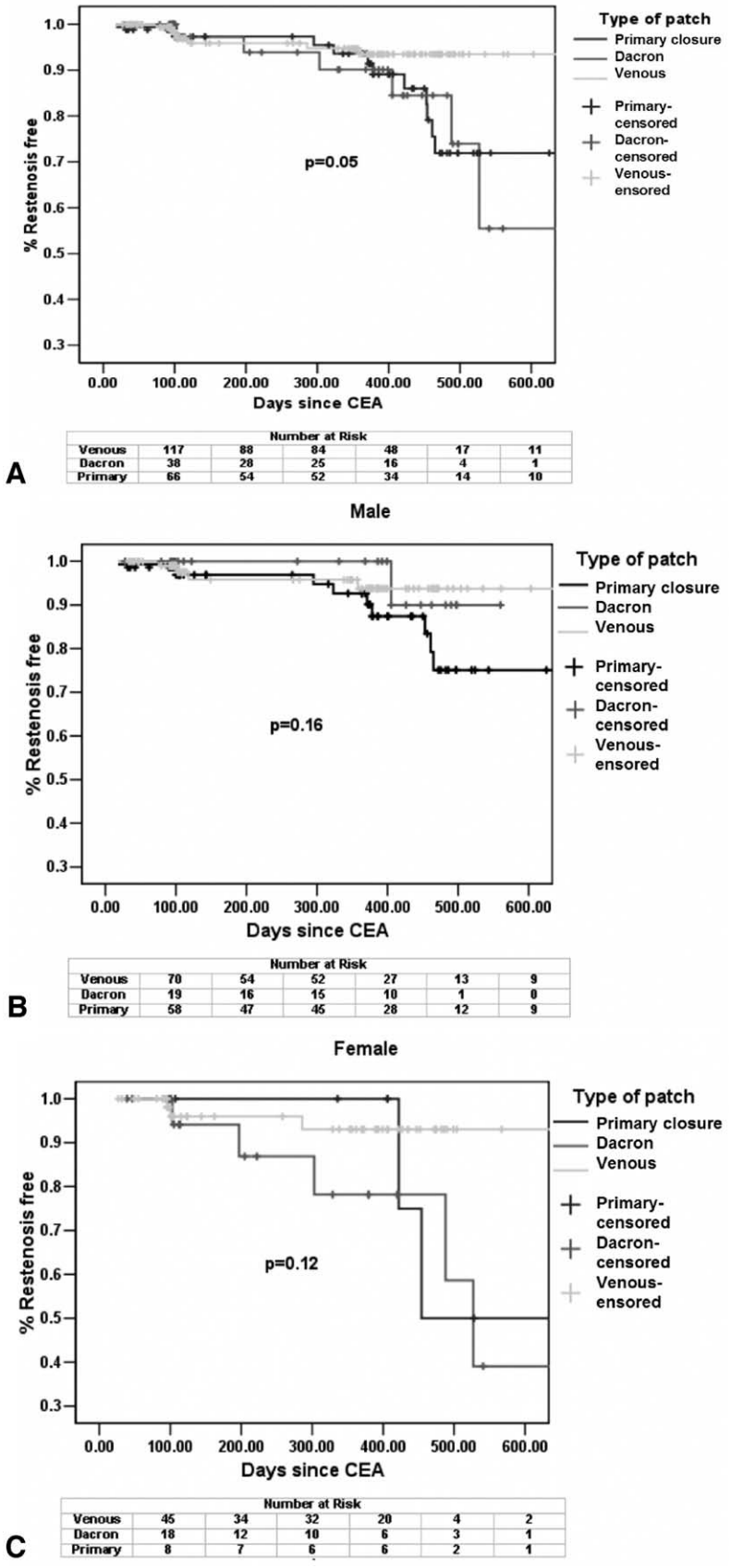

Fig 2. Restinosis free survival in relation to closure technique used during carotid endarterectomy (CEA). Kaplan-Meier curves and estimates are presented for males and females combined **(A)**, for males **(B)**, and for females separately **(C)**.

cerebral events; high numbers of emboli recorded after surgery and during closure of the vessel are also related with adverse outcome.[5,6] The occurrence of emboli may be influenced by the closure technique used, so that the closure technique with less risk of embolism should be preferable. Probably because of the dividing of microemboli in the aforementioned categories, we were able to relate microemboli during wound closure and clamp release to Dacron patches. This relationship was suggested by other authors, but until now no statistical differences have been observed between the different kinds of patch materials and the occurrence of microemboli.[7] The newly described relationship between Dacron patching and the occurrence of microemboli could be explained by the thrombogenic characteristics of this material, as described in earlier studies.[23,24] However, neither these studies nor the current one provides a final answer to the question of whether the cause is mainly thromboembolic or gaseous or a combination of both.

Women have been shown to have an increased number of microemboli recorded after CEA.[6,25] Hayes et al[25] related this increased number of microemboli to the increased risk for stroke in women after CEA, as published by the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial Collaborators.[26,27] Our findings strengthen this hypothesis. The increase of microemboli in female patients might be due to an increased thromboembolic potential in women; this could be related to the influence of estrogen and progestin. The influence of these hormones on the risk for venous thrombosis has been documented.[28] Reiner et al[29] also showed an increased risk for stroke in young women with genetic variants of platelet glycoprotein receptors.

We did not observe a relationship between immediate ischemic cerebral events and the type of patch being used. A recent review[1] suggested such a relationship; therefore, the small number of patients with adverse outcomes in our study could explain our findings. In contrast, we did find a relationship between ischemic events and an increased number of microemboli during the dissection phase of the operation. This was also described in a previous article, but that study also showed a positive relationship between emboli during wound closure and outcome, and we were unable to reproduce this result in the current study.[5] This may also have been caused by the small number of patients with adverse outcomes in our study.

Primary closure and Dacron patch closure were associated with an increased restenosis rate, and sex seemed to modify this outcome strongly. This difference between the sexes might be important and could influence conclusions based on three recently published studies, in which Dacron patch closure was recommended compared with primary closure, but in which sex was not taken into account.[9,30,31] The increased percentage of restenosis for Dacron patches and primary closures could probably be explained by different kinds of arterial remodeling and intimal hyperplasia. In the literature, two types of remodeling are described: inward remodeling, with a consistent outer diameter of the vessel and increasing neointima leading to restenosis, and outward remodeling, with an increase of outer diameter and an increase of neointima but a consistent luminal area.[32] The difference between restenosis after primary closure and venous patching is probably based on the difference in luminal area and, thereby, differences in remodeling mechanisms. The difference in restenosis rates between Dacron patches and venous patches could be explained by the fact that prosthetic grafts lack endothelium. These prosthetic grafts are covered with neointima consisting of fibroblasts and fibrous matrix, which is known to induce intima hyperplasia. Finally, the luminal areas between men and women are also different, and this may contribute to the difference in restenosis rates. The consequences of restenosis after CEA are, however, still uncertain.

Limitations. Because this study was retrospective and randomization between patch materials was not performed, it is conceivable that there are differences in patient characteristics among the groups and that a selection bias led to the use of Dacron patches in patients with more severe disease. However, we studied these characteristics and could not identify such a difference. Additionally, the study was limited by the number of patients with TCD registration in which microemboli were divided into the different phases of CEA, as described previously in this article, and this study did not deal with post-CEA microembolic recordings. Finally, our long-term follow-up was limited. However, the patients will be monitored, and data will become available in the future.

Conclusions. On the basis of our results, avoiding Dacron patches used for closure of the CEA is defendable. Not only was an increased number of microemboli related to Dacron patches, but restenosis was related to Dacron patch closure as well. Thus, venous patch closure and primary closure (in men) may be the preferred techniques.

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